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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,370	10/03/2001	Randall K. Holmes	33,383-00	8568

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/806,370	Applicant(s) Holmes et al
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 3, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-17 and 24-42* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-17 and 24-42* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 18-23 have been canceled.

Claims 1-17, 24-42 are pending.

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

2. The information disclosure statement filed February 5, 2003 has been considered as to the merits.

Claim Objections

3. Claim 24 is objected to because of the following informalities: Claim 24 recites the phrase "a DNA sequence which encode"; it should be --encodes--. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 101

4. Claim 27 provides for the use of a mutant cholera holotoxin, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 27 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 12 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The plasmid DNA encoding HSV gD2 antigen that serves as a polynucleotide vaccine has not been described in the instant specification. Deposit of the plasmid recited in the claims under the Budapest Treaty could enable this claim. No original descriptive support could be found for the DNA sequence being claimed as a vaccine antigenic composition. What has not been described has not been enabled.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-17,24-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-17,24-42 are unclear as no reference sequence is recited in the claims and various locations are set forth in the claims without any specific frame of reference. Various positions may not be present in the A subunit of claim 15 which includes any type of mutation, to include insertions, additions and deletion mutations. Claim 16 depends from claim 15 and defines the mutation to be a substitution, but the mutant of claim 15 has not been defined to comprise the recited positions of claim 16; are the positions present in the A-subunit of claim 15? Absent a

reference sequence, where or what changes have been introduced is unclear in light of the fact that cholera toxin subunit A is known to have sequence variation (see Swiss ProtAccession numbers Q8vLI6, Q8l356, and P01555.)

Claim 2 depends from claim 1 and defines the composition to as "comprising more than one antigen". Claim 1 defines the composition to comprise a single antigen through the recitation of the phrase "a selected antigen". Claim 1 comprises two antigens already, specifically cholera toxin and a parasite antigen. How is claim 2 further limiting of claim 1? Claim 2 should recite --further comprising an additional antigen-- to clearly define the invention. Claim 2 is also unclear in light of the fact that a holotoxin comprises a plurality of epitopes, each being a single antigen; claim 1 is directed to a mutant cholera holotoxin. How is claim 2 further limiting of claim 1?

Claims 3 and 29 recite the phrase "the amino acid at position 29 is histidine". The phrase "amino acid" lacks antecedent basis in claims 1 and 17 from which claims 3 and 29 depend.

Claims 5,31 and 7,33 recite the phrase "or any combination thereof" and "or a combination thereof", respectively. Neither base claim compositions comprise combinations of antigens. Amendment of the base claim to provide for more than one selected antigen would provide antecedent basis for the recitation of these phrases.

Claims 12 and 38 define the antigenic composition to be "a polynucleotide vaccine comprising plasmid DNA encoding HSV gD2". The HSV gD2 antigen recited in claims 11 and 37, respectively, is not defined to be a polynucleotide, but the glycoprotein through the recitation of "gD2". Claims 12 and 38 redefines the antigen to be a polynucleotide and is not further limiting of the claim from which they depend, claims 11 and 37 do not provide antecedent basis for the recitation of the term "polynucleotide". The vaccine of Claims 12 and 38 is defined to be a plasmid DNA encoding HSV g; what plasmid DNA encodes HSV gD2? How does the *plasmid* DNA function as a vaccine? Clarification of the antigenic composition and what is contained in the vaccine is requested.

Claims 14 and 40 define an antigenic composition that comprises an additional adjuvant, but it is not clear that all of the claimed compositions of claim 1 comprise the mutant cholera holotoxin (see rejection of claim 1 above). Amendment of claim 1 to clearly set forth that all of the claimed compositions comprise the mutant holotoxin adjuvant would allow claims 14 and 40 to clearly define the presence of a second adjuvant.

Claims 15 and 41 recite the phrase "at least one additional mutation is made to the A subunit" "at a position other than amino acid 29". The mutation of claim 15 is not required to be any specific type of mutation and would include additions, deletions, insertions or substitutions at any number of locations. What is the resultant molecule in light of the fact that the claim does not require the mutant to evidence adjuvant activity; claim 15 only defines what the starting material is and permits a plurality of mutations with no upper limit? The claim reads on a mutant A subunit of LT with the beta subunits of cholera toxin.

Claims 16 and 42 depend from claims 15 and 41, respectively, and recite various positions for substitution. Claims 15 and 42 do not define type of resultant mutant molecule which may be of any size due to any type of mutation being introduced into the A-subunit. Are the positions recited in claims 16 and 42 present in the composition of claims 15 and 42?

Claim 26 recites the phrase "immunogenic detoxified protein"; the word "protein" lacks antecedent basis in claim 26, which provides antecedent basis for "mutant cholera holotoxin". What detoxified protein is being produced? Clarification of the invention is requested.

9. Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the step of positively expressing the mutant cholera holotoxin and recovering the mutant cholera holotoxin. Claim 26 only requires the culturing of the host cell but the culture medium does not comprise arabinose, which is required for induction of the promoter that controls expression of the mutant cholera holotoxin. How can one be sure the

mutant cholera holotoxin has been produced unless an indicator or recovery step has been carried out? The invention is not distinctly claimed.

Claim 27 does not set forth any specific methods steps. The invention is not distinctly claimed.

Claim Rejections - 35 U.S.C. § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Please Note: Claim 1 recites the phrase "An antigenic composition comprising a selected antigen from a pathogenic **bacterium, virus, fungus**, or *parasite and an effective adjuvanting* amount"; The examiner is reading claim 1 to include at least three types of compositions:

a. one composition being an antigenic composition comprising a selected antigen from a pathogenic bacterium, virus, fungus;

b. another composition being a parasite and an effective adjuvanting amount;

c. and the third composition being a pathogenic bacterium, virus, fungus, or parasite and an effective adjuvanting amount.

11. Claims 1-2,4,6,11,13,17,28,30,32,37-39 are rejected under 35 U.S.C. 102(b) as being rejected by Rappuoli (WO95/17211).

(Instant claim 1, 11) Rappuoli discloses the claimed invention directed to an antigenic composition that comprises an antigen of a pathogenic bacterium (see page 8, lines 24-27), a pathogenic virus (see page 8, lines 15-23), and pathogenic parasites (see protozoan, page 9, lines

4-11). These antigen (see page 18, claims 9, 13-14) include a polynucleotide based vaccine (see page 9, lines 7-11), a whole inactivated or attenuated organism, HSV gD, gB glycoproteins (see page 9, lines 20-29).

Instant claim 2: more than one antigen (see page 10, antigen conjugated to bacterial toxoid, diphtheria, tetanus, cholera, H.pylori) as a carrier.

Instant claims 4, 6 and 11,: selected antigen is Helicobacter pylori urease(see page 8, line 26; and page 9, line 24, 28-29, whole cells comprise urease) or HSV gD glycoproteins (see page 9, line 21; lines 28-29, gD2 is included in the genus of gD glycoproteins).

Instant claim 13: further comprises a diluent or carrier (see page 11, lines 15-28, specifically line 17 and line 28).

Instant claim 17,28,30, 32, 37-39 : administering the antigenic composition to a host (see page 18, claim 10; page 19, claims 11-12). Inherently the reference anticipates the instantly claimed invention.

12. Claims 1-2, 4-5, 13,17,28, 30-31,and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by St. Geme, III et al (US Pat. 6,245,337).

(Instant claims 1,4 and 5) St. Geme, III et al disclose the claimed invention directed to antigenic compositions of Haemophilus influenzae Hap adherence and penetration antigen (see title, col. 2, lines 59-63).

Instant claims 2 and 13: the compositions further comprise a diluent (col. 14, lines 39-54) or carrier (the carrier being a bacterial, fungal, or eukaryotic host cell, and would therefore comprise more than one antigen (see col. 9, lines 35-44).

Instant claim 17,28,30-31, 39: administration of the composition to a host is also disclosed (see col. 14, lines 55-61; claims 4-5, col. 73-74) . The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a mutant holotoxin, the mutation being a substitution at position 29.

13. Claims 1-2, 4, 11-13, 17, 28,30, 37-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Burke et al (US Pat. 5,171,568).

Instant claims 1,4,11-12: Burke et al disclose the claimed invention directed to antigenic compositions of HSV gD2 antigen (see col. 3, line 11; col. 3, lines 4-17; plasmid pBr322, col. 7, lines 32-68 and col. 8, lines 1-10).

Instant claim 2: comprising more than one antigen (see col. 33, lines 35-36, gD and gB antigens of HSV administered together with an adjuvant (see col. 33, lines 33-50)

Instant claim 13: the compositions further comprise a carrier (col. 2, line 63-64; col. 51, sections 5.1-51; see claims 10, 11 and 15-23).

Instant claim 17,28, 30,37-39: the composition is administered to a host (see col. 32, section 6.1, lines 60-68; see col. 44, claim 13, and claims 3,5, and 6). The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a holotoxin.

14. Claims 1-2, 4, 6, 13, 17, 28, 30,32, 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Michetti et al (US Pat. 5,972,336).

(Instant claims 1,4,6) Michetti et al disclose the claimed invention directed to antigenic compositions of Helicobacter pylori urease (see title).

Instant claim 2: further comprising more than one antigen (see claims 1-26; Helicobacter pylori urease together with cholera toxin (see claim 6).

Instant claim 13: the compositions further comprise a carrier or diluent (see claims 8-10, and 21).

Instant claim 17, 28, 30,32, 39 the composition is administered to a host (see claims 1-26). The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a mutant holotoxin, the mutation being a substitution at position 29.

15. Claims 1-2, 4, 6, 9, 13, 17,28, 30,32, 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Michetti et al (US Pat. 6,290,962).

(Instant claims 1,4,6) Michetti et al disclose the claimed invention directed to antigenic compositions of Helicobacter pylori urease (see title).

Instant claim 2: further comprising more than one antigen (see together with cholera toxin, fungal polysaccharide, rotavirus-like particles (see col. 12, lines 16-51, and claims 1-72).

Instant claim 9: rotavirus like particles (see col.36, claim 20)

Instant claim 13: the compositions further comprise a carrier or diluent (see claims 62-65).

Instant claim 17,28, 30,32, 39 the composition is administered to a host (see claims 71-72). The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a mutant holotoxin, the mutation being a substitution at position 29.

16. Claims 1, 2, 4 , 9-10, 13, 17, 28, 30,35-36 are rejected under 35 U.S.C. 102(a) as being anticipated by O'Neal et al (April 1998).

O'Neal et al disclose a combination composition that comprises rotavirus virus like 2/6 particles, the two different particles presenting at least first and second rotavirus like antigens (proteins). The first and second antigens were additionally combined with cholera or E.coli heat-labile toxin bacterial antigen.

The reference also discloses a method of enhancing the immune response of a host, the method comprising the step of administering the antigenic composition to a host. O'Neal et al anticipates the instantly claimed invention. The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a mutant holotoxin, the mutation being a substitution at position 29.

17. Claims 1,2,4,7,13, 17, 28,30,33,39 are rejected under 35 U.S.C. 102(e) as being anticipated by Zollinger et al (US Pat. 6,558, 677).

(Instant claim 1) Zollinger et al disclose the claimed invention directed to an antigenic composition that comprises Neisseria meningitidis PorA (see claims 1-2, col. 18, line 17).

Instant claim 2: the composition comprised an additional antigen (see claim 2, at least one antigen chosen from 5 different Neisseria antigens).

Instant claims 4 and 7: PorA antigen of Neisseria meningitidis group B (see col. 3, lines 23-28, and claims 1-2).

Instant claim 13: further comprises a carrier or diluent (see col. 3, line 22, 28, 64-65).

Instant claim 17, 28,30,33,39: administers the antigenic composition to a host (see claims 1-5).

The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a mutant holotoxin, the mutation being a substitution at position 29.

18. Claims 1-2, 17,28,39 are rejected under 35 U.S.C. 102(e) as being anticipated by Arntzen et al (US Pat. 6,395,964; filing date August 4, 1997).

Instant claims 1-2: Arntzen et al disclose an antigenic composition that comprises a microorganism antigen (bacteria, fungi, protozoa or viruses,see col. 11, lines 4-5) together with one or more antigens (col. 18 lines 35-43), the second antigen being a mutant cholera holotoxin, the mutant holotoxin being one with substitutions of amino acid codons to facilitate expression of the recombinant cholera toxin in plants (see col. 12, lines 49-55). Plant codons were substituted for native cholera toxin codons to facilitate expression in a transformed plant cell. The bacteria, fungi, protozoa or viruses antigens are expressed together with the mutant cholera holotoxin through coordinated coexpression (see col. 12, lines 62-67 and col. 14, lines 17-18) of the additional microorganism antigen (see abstract).

An additional embodiment disclosed is an antigenic composition that comprises LT-A and CT-B (plants or plant tissues transformed and expressing synthetic DNA encoding the antigens) (see col. 18, lines 23-26) together with an antigen from a pathogen, such as a virus(see col. 17, lines 29-30; col. 1, lines 28-37 and lines 49-67; col. 4, lines 54-67) .

The reference discloses a method that comprises the step of administering the composition to a host (see title, abstract).

The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a mutant holotoxin, the mutation being a substitution at position 29.

19. Claims 1-2, 4-8, 13, 17 28,30-34,39 are rejected under 35 U.S.C. 102(e) as being anticipated by Gizurarson et al (US Pat. 6,514,503).

(Instant claims 1,4-8) Gizurarson et al disclose the claimed invention directed to antigenic compositions of bacterial, viral or fungal antigens (see col. 7, lines 5-19), to include specific antigens from Haemophilus influenzae P4 outer membrane protein (see Example X, col. 18, lines 57-67 and claims); Helicobacter pylori urease (see col. 19, Example XI, lines 48-67 and col. 20, lines 1-9 and claims); Neisseria meningitidis pilin (rpilin, see Example XII, col. 20, lines 14-45, and claims); respiratory syncytial virus (see col. 6, line 59; also see claim 15.)

Instant claim 2: further comprising more than one antigen (combinations of antigens, see col. 11, lines 64-67 and col. 12, lines 1-9).

Instant claim 13: the compositions further comprise a carrier or diluent (see col. 9, line 45; col. 9, lines 3-37, col. 10, lines 6-67).

Instant claim 17, 28,30-34,39: the composition is administered to a host (see col. 12, lines 9-28; col. 8, lines 55-67). The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a mutant holotoxin, the mutation being a substitution at position 29.

20. Claims 1-2, 4-5, 13, 17, 28,30-31,39 are rejected under 35 U.S.C. 102(e) as being anticipated by Chong et al (US Pat. 5,679,352).

(Instant claims 1,4-5) Chong et al disclose the claimed invention directed to antigenic compositions of antigens from Haemophilus influenzae P6 outer membrane protein (see claim 5 and abstract).

Instant claim 2: further comprising more than one antigen (combinations of antigens, see claim 5, first and second epitopes; epitopes are antigens).

Instant claim 13: the compositions further comprise a carrier (see claim 7).

Instant claim 17, 28,30-31,39: the composition is administered to a host (see claim 8). The reference anticipates the instantly claimed antigenic compositions that do not require the presence of a mutant holotoxin, the mutation being a substitution at position 29.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp June 27, 2003

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